

## PATENT

*(C) O'NELL*  
in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a SV40tsA58 gene.

*F2*  
*E2*  
7. (Thrice Amended) A neuronal cell line obtained from a transgenic rat, the cells of which comprise:

- (i)* a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to  
*(ii)* a cell type specific promoter and in which the conditional oncogene, transforming gene, immortalizing gene or the cell cycle affecting gene is a C Erb  $\beta$  2 gene or a TGF  $\alpha$  gene.

8. (Twice Amended) A cell line as claimed in claim 7 in which the cell type specific promoter is a human NF-L gene promoter.

*Sudha F 28*  
*E3*  
13. (Twice Amended) A method of producing a transgenic rat, comprising:

- (i)* causing a female rat to super-ovulate by supplying her with a regular supply of Follicle Stimulating Hormone (FSH) prior to mating;  
*(ii)* mating or artificially inseminating the female rat;  
*(iii)* obtaining the resulting embryo from the female rat; and  
*(iv)* incorporating  
*(i)* a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to  
*(ii)* a cell specific promoter into the genome of the rat embryo in which the conditional oncogene, transforming gene or immortalizing gene or the cell

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*E3 F3 CDR +*  
cycle affecting gene is a SV40tsA58 gene, C Erb  $\beta$  2 gene or a TGF  $\alpha$  gene.

17. (Twice Amended) A transgenic rat whose germ cells and somatic cells contain

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter as a result of chromosomal incorporation into the rat genome or into the genome of an ancestor of said rat in which the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting gene is a SV40tsA58 gene.

18. (Twice Amended) A transgenic rat whose germ cells and somatic cells contain

(i) a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to

(ii) a cell type specific promoter as a result of chromosomal incorporation into the rat genome or into the genome of an ancestor of said rat, wherein the conditional oncogene, transforming gene, immortalizing gene, or the cell cycle affecting gene is a C Erb  $\beta$  2 gene or a TGF  $\alpha$  gene.

25. (Amended) A method of generating a cell line from a transgenic rat comprising a conditional oncogene, transforming gene or immortalizing gene or a cell cycle affecting gene operably linked to a cell specific promoter, the method comprising:

(i) maintaining the rat at restrictive conditions such that the conditional oncogene, transforming gene or immortalizing gene or the cell cycle affecting

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*(b) Confidential*  
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*CONT.*

gene is a SV40tsA58 gene, a C Erb  $\beta$  2 gene, or a TGF  $\alpha$  gene and is expressed in vivo, only in a tissue of interest and in an inactive form such that the cells thereof grow normally;

- (ii) culturing said cells from the tissue of interest in vitro under permissive conditions such that the immortalizing function is activated; and
- (iii) subjecting the cells to non-permissive conditions so as to result in a cessation of growth and in differentiation.

*B6*

29. (Amended) A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising administering said material to a rat produced according to the method of claim 13 or an ancestor thereof and detecting a reduced incidence of development of neoplasms, compared to an untreated rat, as an indication of said protection.

*E7*

30. (Amended) The method of claim 13 wherein and wherein the cell type specific promoter is a human NF-L gene promoter.

*E8*

32. (Amended) The method of claim 25 wherein the cell type specific promoter is a human NF-L gene promoter.

REMARKS

Before amendment, claims 1, 4, 6-9, 13 and 15-32 were pending. After amendment, claims 1, 4, 7-9, 13 and 15-32 are pending.

A marked up of the claims indicating the changes made as a result of this amendment is attached.